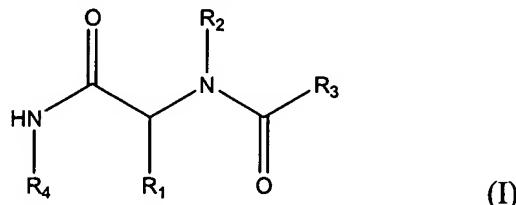


CLAIMS

What is claimed is:

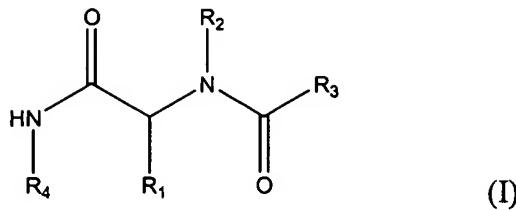
- 5 1. A method of inhibiting tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by Formula (I):



or a physiological salt thereof, wherein:

- 10 R₁ is a substituted or unsubstituted aryl group or a substituted or unsubstituted alkyl group;
- R₂ is an optionally substituted aralkyl group or an alkyl group substituted with -NR₅R₆;
- R₃ is a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group;
- 15 R₄ a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group; and
- R₅ and R₆ are independently selected from a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group or R₅ and R₆ taken together with the nitrogen to which they are attached are a non-aromatic heterocyclic group.

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2. A method of inhibiting chronic tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by Formula (I):



or a physiological salt thereof, wherein:

R₁ is a substituted or unsubstituted aryl group or a substituted or unsubstituted alkyl group;

5 R₂ is an optionally substituted aralkyl group or an alkyl group substituted with -NR₅R₆;

R₃ is a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group;

10 R₄ a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group; and

R₅ and R₆ are independently selected from a substituted or unsubstituted alkyl group or a substituted or unsubstituted aryl group or R₅ and R₆ taken together with the nitrogen to which they are attached are a non-aromatic heterocyclic group.

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3. The method of Claim 2 wherein R₂ is an optionally substituted heteroaralkyl group or an alkyl group substituted with -NR₅R₆.

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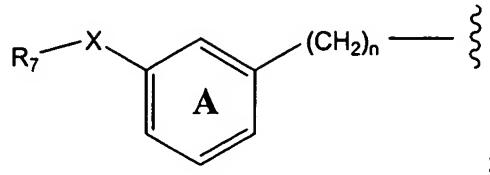
4. The method of Claim 3 wherein R₄ is an optionally substituted aryl group, an optionally substituted cycloalkyl group, an optionally substituted C₁-C₄ aralkyl group or an optionally substituted C₁-C₄ cycloalkylalkyl group.

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5. The method of Claim 4 wherein R₄ is an optionally substituted phenyl group, an optionally substituted phenyl-C₁-C₄-alkyl group, an optionally substituted diphenyl-C₁-C₄-alkyl group, an optionally substituted C₃-C₈-cycloalkyl-C₁-C₄-alkyl group or an optionally substituted di-(C₃-C₈-cycloalkyl)-C₁-C₄-alkyl group.

6. The method of Claim 5 wherein R₄ is an optionally substituted benzyl, an optionally substituted diphenylmethyl, an optionally substituted 2-phenylethyl, an optionally substituted 1,2-diphenylethyl, an optionally substituted 2,2-diphenylethyl or an optionally substituted 3,3-diphenylpropyl.
- 5
7. The method of Claim 3 wherein R₁ is an optionally substituted aryl group or an optionally substituted C₁-C₄ aralkyl group.
- 10 8. The method of Claim 7 wherein R₁ is an optionally substituted phenyl group or an optionally substituted phenyl-C₁-C₄ alkyl group.
- 15 9. The method of Claim 3 wherein R₃ is an optionally substituted aryl group or an optionally substituted C₁-C₄ aralkyl group.
10. The method of Claim 9 wherein R₃ is an optionally substituted phenyl, an optionally substituted phenyl-C₁-C₄-alkyl, an optionally substituted diphenyl-C₁-C₄-alkyl, an optionally substituted pyrazolyl, an optionally substituted pyrazolyl-C₁-C₄-alkyl, an optionally substituted indolyl, an optionally substituted indolyl-C₁-C₄-alkyl, thienylphenyl, thienylphenyl-C₁-C₄-alkyl, furanylphenyl, furanylphenyl-C₁-C₄-alkyl, an optionally substituted fluorenyl, an optionally substituted fluorenyl-C₁-C₄-alkyl, an optionally substituted naphthyl, an optionally substituted naphthyl-C₁-C₄-alkyl, an optionally substituted quinoxalinyl, an optionally substituted quinoxalinyl-C₁-C₄-alkyl, an optionally substituted quinazolinyl, an optionally substituted quinazolinyl-C₁-C₄-alkyl, an optionally substituted pyrrol, an optionally substituted pyrrol-C₁-C₄-alkyl, an optionally substituted thienyl, an optionally substituted thienyl-C₁-C₄-alkyl, an optionally substituted furanyl, an optionally substituted furanyl-C₁-C₄-alkyl, an optionally substituted pyridyl or an optionally substituted-C₁-C₄ pyridyl.
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11. The method of Claim 10 wherein R₃ is represented by the following structural formula:



5 wherein Ring A substituted or unsubstituted; R₇ is an optionally substituted phenyl, optionally substituted furanyl, optionally substituted thieryl or optionally substituted pyridyl group; n is an integer from 1-4; and X is a bond, CH₂, OCH₂, CH₂OC(O), CO, OC(O), C(O)O, O, S, SO or SO₂.

12. The method of Claim 3 wherein R₃ is an optionally substituted an optionally substituted 2-cyclohexylethyl, an optionally substituted 2-cyclopentylethyl, or 10 an optionally substituted C₃-C₈ secondary or tertiary alkyl group.

13. The method of Claim 3 wherein R₂ is an optionally substituted 2-(imidazol-4-yl)ethyl, an optionally substituted 3-(imidazol-4-yl)propyl, an optionally substituted 3-(imidazol-1-yl)propyl, an optionally substituted 2-(morpholin-4-yl)ethyl, an optionally substituted 2-(4-pyrazolyl)ethyl, an optionally substituted 2-N,N-dimethylaminoethyl or an optionally substituted 3-N,N-dimethylaminopropyl. 15

- 20 14. The method of Claim 3 wherein:
- a) R₁ is an optionally substituted aryl group or an optionally substituted C₁-C₄ aralkyl group;
 - b) R₃ is an optionally substituted aryl group or an optionally substituted C₁-C₄ aralkyl group; and
 - c) R₄ is an optionally substituted aryl group, an optionally substituted cycloalkyl group, an optionally substituted C₁-C₄ aralkyl group or an 25 optionally substituted C₁-C₄ cycloalkylalkyl group.

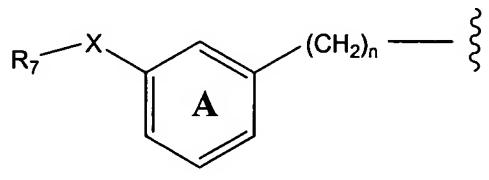
15. The method of Claim 3 wherein:

- a) R₁ is an optionally substituted phenyl group or an optionally substituted phenyl-C₁-C₄ alkyl group;
- 5 b) R₃ a substituted or unsubstituted phenyl, phenyl-C₁-C₄-alkyl, diphenyl-C₁-C₄-alkyl, pyrazolyl, pyrazolyl-C₁-C₄-alkyl, indolyl, indolyl-C₁-C₄-alkyl, thienylphenyl, thienylphenyl-C₁-C₄-alkyl, furanylphenyl, furanylphenyl-C₁-C₄-alkyl, fluorenlyl, fluorenlyl-C₁-C₄-alkyl, naphthyl, naphthyl-C₁-C₄-alkyl, quinoxalinyl, quinoxalinyl-C₁-C₄-alkyl, an optionally substituted quinazolinyl, an optionally substituted quinazolinyl-C₁-C₄-alkyl, pyrolyl, pyrolyl-C₁-C₄-alkyl, thienyl, thienyl-C₁-C₄-alkyl, furanyl or furanyl-C₁-C₄-alkyl; and
- 10 c) R₄ is an optionally substituted phenyl group, an optionally substituted phenyl-C₁-C₄-alkyl group, an optionally substituted diphenyl-C₁-C₄-alkyl group, an optionally substituted C₃-C₈-cycloalkyl-C₁-C₄-alkyl group or an optionally substituted di-(C₃-C₈-cycloalkyl)-C₁-C₄-alkyl group.

16. The method of Claim 15 wherein R₂ is an optionally substituted imadazolyl-C₁-C₄-alkyl group or a C₁-C₄ alkyl group substituted with -NR₅R₆.

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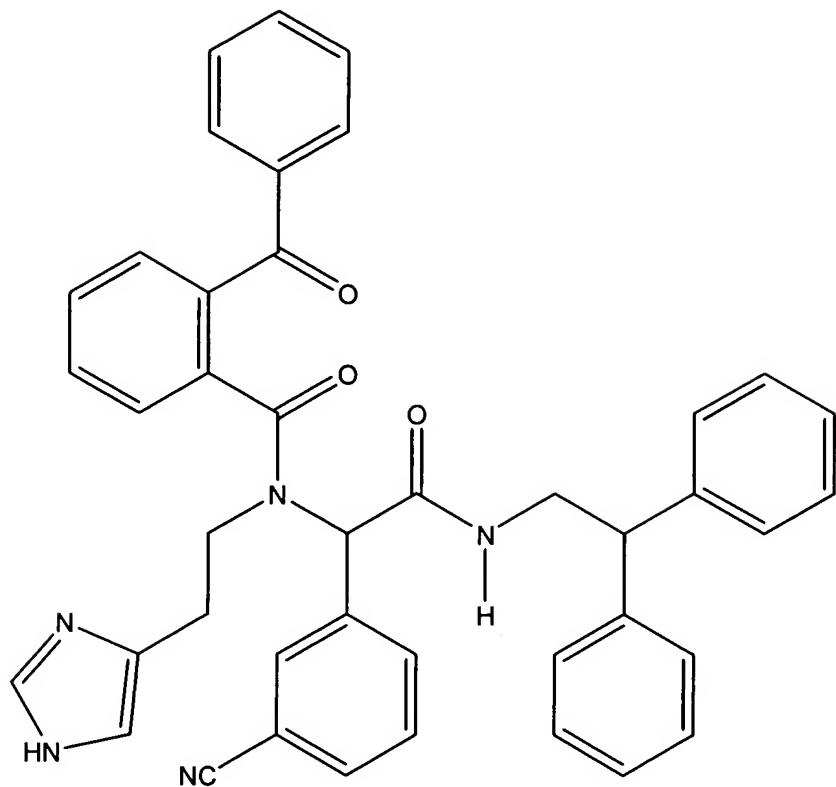
17. The method of Claim 16 wherein R₃ is represented by the following structural formula:



25 wherein Ring A substituted or unsubstituted; R₇ is an optionally substituted phenyl, furanyl, thienyl or pyridyl group; n is an integer from 1-4; and X is a bond, CH₂, OCH₂, CH₂OC(O), CO, OC(O), C(O)O, O, S, SO or SO₂.

18. The method of Claim 17 wherein R₄ is 2,2-diphenylethyl, 2-phenylethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, benzyl, or 2-pyridylethyl, each optionally substituted with -OH, halogen, R, -CH₂R, -OCH₂R, -CH₂OC(O)R, -OR, -O-COR, -COR, -CN, -NO₂, -COOH, -SO₃H, -NH₂, -NHR, -N(R)₂, -COOR, -CHO, -CONH₂, -CONHR, -CON(R)₂, -NHCOR, -NRCOR, -NHCONH₂, -NHCONRH, -NHCON(R)₂, -NRCONH₂, -NRCONRH, -NRCON(R)₂, -C(=NH)-NH₂, -C(=NH)-NHR, -C(=NH)-N(R)₂, -C(=NR)-NH₂, -C(=NR)-NHR, -C(=NR)-N(R)₂, -NH-C(=NH)-NH₂, -NH-C(=NH)-NHR, -NH-C(=NH)-N(R)₂, -NH-C(=NR)-NH₂, -NH-C(=NR)-N(R)₂, -NRH-C(=NH)-NH₂, -NR-C(=NH)-NHR, -NR-C(=NR)-N(R)₂, -SO₂NH₂, -SO₂NHR, -SO₂N(R)₂, -SH or -SO_kR;
- each R is independently C₁-C₄ alkyl or phenyl optionally substituted with amino, alkylamino, dialkylamino, aminocarbonyl, halogen, alkyl, alkylaminocarbonyl, dialkylaminocarbonyloxy, alkoxy, nitro, cyano, carboxy, alcoxycarbonyl, alkylcarbonyl, hydroxy, haloalkoxy, or haloalkyl; and
- k is zero, one or two.
19. The method of Claim 18 wherein R₁ is a phenyl group or phenyl-C₁-C₄ alkyl group each optionally substituted with R, -CH₂R, -OCH₂R, -CH₂OC(O)R, -OH, halogen, -OR, -O-COR, -COR, -CN, -NO₂, -COOH, -SO₃H, -NH₂, -NHR, -N(R)₂, -COOR, -CHO, -CONH₂, -CONHR, -CON(R)₂, -NHCOR, -NRCOR, -NHCONH₂, -NHCONRH, -NHCON(R)₂, -NRCONH₂, -NRCONRH, -NRCON(R)₂, -C(=NH)-NH₂, -C(=NH)-NHR, -C(=NH)-N(R)₂, -C(=NR)-NH₂, -C(=NR)-NHR, -C(=NR)-N(R)₂, -NH-C(=NH)-NH₂, -NH-C(=NH)-NHR, -NH-C(=NR)-N(R)₂, -NRH-C(=NH)-NH₂, -NR-C(=NH)-NHR, -NR-C(=NH)-N(R)₂, -NR-C(=NR)-NH₂, -NR-C(=NR)-NHR, -NR-C(=NR)-N(R)₂, -SO₂NH₂, -SO₂NHR, -SO₂N(R)₂, -SH or -SO_kR.

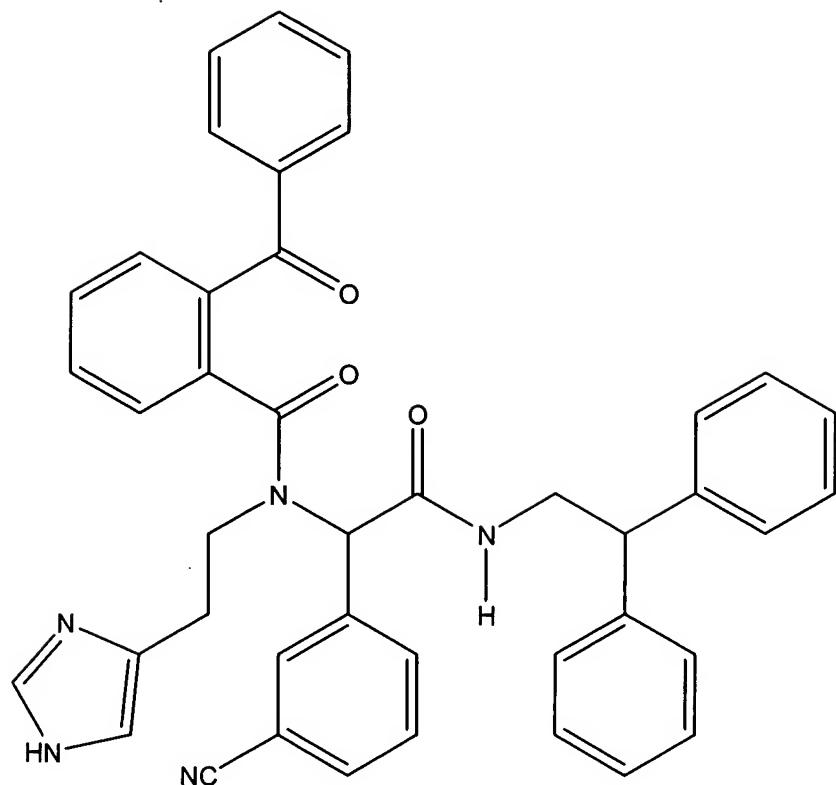
20. The method of Claim 19 wherein R₁ is a phenyl group or phenyl-C₁-C₂ alkyl group, each optionally substituted with C₁-C₄ alkyl, C₁-C₄ alkoxy, halogen, CN, C₁-C₄-alkylthiol, C₁-C₄-haloalkyl or phenoxy; R₄ is 2,2-diphenylethyl, 2-phenylethyl, benzyl, diphenylmethyl, 1,2-diphenylethyl, 3,3-diphenylpropyl, benzyl, or 2-pyridylethyl, each optionally substituted with C₁-C₄ alkyl, C₁-C₄ alkoxy, halogen, CN, C₁-C₄-alkylthiol, C₁-C₄-haloalkyl or phenoxy; R₇ is an 5 optionally substituted phenyl group; n is 1; and X is CO.
21. The method of Claim 20 wherein Ring A is unsubstituted and R₇ is a phenyl group optionally substituted with R, -CH₂R, -OCH₂R, -CH₂OC(O)R, -OH, 10 halogen, -OR, -O-COR, -COR, -CN, -NO₂, -COOH, -SO₃H, -NH₂, -NHR, -N(R)₂, -COOR, -CHO, -CONH₂, -CONHR, -CON(R)₂, -NHCOR, -NRCOR, -NHCONH₂, -NHCONRH, -NHCON(R)₂, -NRCONH₂, -NRCONRH, 15 -NRCON(R)₂, -C(=NH)-NH₂, -C(=NH)-NHR, -C(=NH)-N(R)₂, -C(=NR)-NH₂, -C(=NR)-NHR, -C(=NR)-N(R)₂, -NH-C(=NH)-NH₂, -NH-C(=NH)-NHR, -NH-C(=NH)-N(R)₂, -NRH-C(=NH)-NH₂, -NR-C(=NH)-NHR, -NR-C(=NH)-N(R)₂, -NR-C(=NR)-NH₂, -NR-C(=NR)-NHR, -NR-C(=NR)-N(R)₂, -SO₂NH₂, 20 -SO₂NHR, -SO₂N(R)₂, -SH or -SO_kR.
22. The method of Claim 21 wherein R₇ is a phenyl group.
23. The method of Claim 22 wherein R₂ is 2-(imidazol-4-yl)ethyl.
- 25 24. A method of inhibiting tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by the following structural formula:



or a pharmaceutically acceptable salt thereof.

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25. A method of inhibiting chronic tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by the following structural formula:



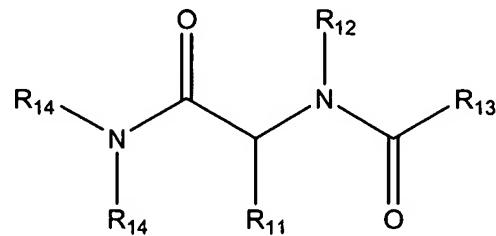
(II).

or a pharmaceutically acceptable salt thereof.

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26. A method of inhibiting tissue transplant rejection in a subject with a tissue transplant, said method comprising the step of administering an effective amount of a compound represented by the following structural formula:

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or a physiologically acceptable salt thereof, wherein:

R₁₁ is -H, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted heteroaryl or a substituted or unsubstituted heteroaralkyl;

5 R₁₂ is alkyl substituted with NR₁₅R₁₆, a substituted or unsubstituted aryl, a substituted or unsubstituted heteroaralkyl, or a substituted or unsubstituted heterocycloalkylalkyl;

R₁₃ is a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, a substituted or unsubstituted aralkyl, a substituted or unsubstituted cycloalkylalkyl, a substituted or unsubstituted heteroaryl, a substituted or unsubstituted heteroaralkyl, a substituted or unsubstituted benzophenonyl, or a substituted or unsubstituted cycloalkylalkyl; and

10 each R₁₄ is independently, -H, a substituted or unsubstituted alkyl, a substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a substituted or unsubstituted heteroaralkyl;

15 R₁₅ and R₁₆ are independently selected from H, a substituted or unsubstituted alkyl, a substituted or unsubstituted cycloalkyl, a substituted or unsubstituted aryl or unsubstituted aralkyl or R₁₃ and R₁₄ together with the nitrogen to which they are attached are a heterocycloalkyl.